REMARKS

Claims 1-26 and 34-47 are pending in the subject application. Claims 16-17, 19-23, 34-41 and 47 have been canceled as withdrawn from further consideration. Applicant has canceled claim 9 without prejudice and amended claims 25 and 43 to introduce certain formatting changes. Applicant maintains that the amendments to the claims do not introduce an issue of new matter. Accordingly, claims 1-8, 10-15, 18, 24-26 and 42-46 will be pending and under examination in the subject application upon entry of this Amendment.

Applicant respectfully requests that, in view of the remarks made herein, the Examiner withdraw the outstanding rejections.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claim 9 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In response to the rejection of claim 9, applicant respectfully points out that claim 9 has been canceled without prejudice, rendering the rejection thereof moot.

In view of the above remarks, applicant respectfully requests the Examiner withdraw the rejection under 35 U.S.C. §112, second paragraph.

Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 1-15, 18, 24-26, and 42-46 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

In response to the rejection of claim 9, applicant respectfully points out that claim 9 has been canceled without prejudice, rendering the rejection thereof moot.

In response to the Examiner's rejection of claims 1-8, 10-15, 18, 24-26 and 42-46, applicants respectfully traverse for the reasons set forth below.

The Legal Standard for Written Description

35 U.S.C. §112, first paragraph, states that "[t]he specification shall contain a *written description* of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, ..." (emphasis added).

The first paragraph of §112 "requires a 'written description of the invention' which is separate and distinct from the enablement requirement. ... [T]he applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed." Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991) (emphasis in original).

An applicant can show possession of a claimed invention "by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention." M.P.E.P. 2163(I), citing *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Consistent with this notion is that "[a]n adequate written description of the invention may be shown by *any description of sufficient, relevant, identifying characteristics* so long as a person skilled in the art would recognize that the inventor had possession of the invention." M.P.E.P. 2163(II)(A)(3)(a) (emphasis added). For example, "[a]n applicant may show that an invention is complete by disclosure of sufficiently detailed, relevant *identifying characteristics* which provide evidence that applicant was in possession of the claimed invention." *Id.* (emphasis added). These "identifying characteristics" include, for example, "*binding affinity [and] binding specificity." Id.* (emphasis added).

The Specification Provides a Written Description of the Claimed Invention

Briefly, claims 1-6 provide a chimeric protein for inhibiting the expression of a gene comprising a DNA methyltransferase whose DNA-binding activity is attenuated relative to that of naturally occurring DNA methyltransferase and a DNA binding protein linked thereto that binds to the gene's promoter suequence under conditions permitting the methylation of a methylation site within the promoter of the gene, thus inhibiting expression of

the gene. Claims 11-15, 18, 24-26 and 29 provide a method for inhibiting expression of a gene which comprises contacting the gene with a chimeric protein for inhibiting the expression of a gene comprising a DNA methyltransferase whose DNA-binding activity is attenuated relative to that of naturally occurring DNA methyltransferase and a DNA binding protein linked thereto, so as to methylate the promoter, thus inhibiting expression of the gene. Claims 7, 8, and 10 provide an expression vector encoding a chimeric protein for inhibiting the expression of a gene comprising a DNA methyltransferase whose DNA-binding activity is attenuated relative to that of naturally occurring DNA methyltransferase and a DNA binding protein linked thereto. Claims 42 and 43 provide a host cell comprising an expression vector encoding a chimeric protein for inhibiting the expression of a gene comprising a DNA methyltransferase whose DNA-binding activity is attenuated relative to that of naturally occurring DNA methyltransferase and a DNA binding protein linked thereto. Claims 44-46 provide a pharmaceutical composition comprising a therapeutically effective amount of an expression vector encoding a chimeric protein for inhibiting the expression of a gene comprising a DNA methyltransferase whose DNA-binding activity is attenuated relative to that of naturally occurring DNA methyltransferase and a DNA binding protein linked thereto and a pharmaceutically acceptable carrier.

The claimed invention is based on applicant's *surprising* discovery that a chimeric protein comprising a DNA methyltransferase whose DNA-binding activity is attenuated relative to that of naturally occurring DNA methyltransferase and a DNA binding protein linked thereto can methylate a methylation site within the promoter of a gene and thus inhibit expression of the gene.

In support of the rejection, the Examiner asserts that the specification does not fully describe the genus of claimed chimeric proteins. In essence, the Examiner asserts that the specification does not disclose the structure of the species of the claimed genus of chimeric proteins in that it fails to describe any representative species by any identifying characteristics or properties other that the functionality of. In addition the Examiner relies on UC California v. Eli Lilly, 43 USPQ2d 1398, in further support of the written description rejection.

In response, applicant maintains that the specification provides written description for the subject matter claimed. First, it is unnecessary that applicant set forth all possible chimeric proteins for establishing written description, or enablement for that matter. Rather, all that need be provided is a representative number of such chimeric proteins. Applicants maintain that a representative number of examples and their specific design and selection have been set forth in the specification. Specifically, as the Examiner has acknowledged, "[t]he specification provides guidance in the form of ... 2 working examples of the claimed chimeric protein - a mutant S.SssI linked via a 9 amino acid linker to a mutant LexA binding protein (see Example 3) for use in inhibiting expression from an HIV 5'-LTR (Examples 5 and 7) and Hepatitis B virus (Example 6)" at, *inter alia*, page 44, line 24 to page 47, line 12, and page 52, line 34 to page 54, line 13. In addition, at *inter alia*, pages 39-57 of the specification, applicant has described in sufficient detail the design, selection and affinity maturation of other chimeric proteins.

Applicant further notes that, contrary to the Examiner's position, no structure/function relationship need be established

for the claimed invention to be adequately described. Indeed, it is sufficient for written description that (i) applicant has provided working examples of the chimeric proteins and (ii) that applicant has described how to design and select chimeric proteins without undue experimentation. In addition, applicant maintains that the text of UC California v. Eli Lilly quoted by the Examiner is inapplicable in this case, as it relates to "claims to genetic material" unique to a given species or class, and not to chimeric proteins such as those claimed here.

It is stressed that *not a single chemical structure* of a compound need be shown in order for the invention to be adequately described. That is, chemical structure is only one of many parameters that may be used to describe the physical nature of a compound. Other parameters include, for example, molecular weight, electronic charge, IR spectrum, UV spectrum, NMR spectrum, mass spectrometry, optical activity, fluorescence, catalytic activity, and of course, binding affinity and specificity. In this case, binding affinity and specificity suffice to describe the compounds claimed. Knowledge of the compounds' chemical structures is not needed to practice the claimed invention, in the same way knowledge of the compounds' IR or UV spectra is also not needed.

Accordingly, applicant maintains that the subject matter of the rejected claims is adequately described in the specification.

The Examiner also rejected claims 1-15, 18, 24-26, and 42-46 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response to the rejection of claim 9, applicant respectfully points out that claim 9 has been canceled without prejudice rendering the rejection thereof moot.

In response to the Examiner's rejection of claims 1-8, 10-15, 18, 24-26 and 42-46, applicants respectfully traverse. Applicant's traversal is based, where applicable, on the reasons set forth in response to the Examiner's written description rejection, and on the following reasons.

The Legal Standard for Enablement

35 U.S.C. §112, first paragraph, states that "[t]he specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to *enable* any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, ..." (emphasis added). "Enablement ... is determined as of the filing date of the patent application." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81 (Fed. Cir. 1986).

"Enablement is not precluded by the necessity for some experimentation such as *routine screening*. However, experimentation needed to practice the invention must not be undue experimentation. ... The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. The term 'undue experimentation' does not appear in the statute, but it is well established that enablement requires that the specification

teach those in the art to make and use the invention without undue experimentation. Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations. ... Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (emphasis added, footnotes omitted).

"[I]t is not necessary that a court review all the *Wands* factors to find a disclosure enabling. They are illustrative, not mandatory. What is relevant depends on the facts ..." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1213 (Fed. Cir. 1991).

The Claimed Invention is Enabled

In support of the rejection, the Examiner asserts that it would require undue experimentation to make and use the claimed invention. Specifically the Examiner asserts that in view of the factors detailed in In re Wands, undue experimentation would be necessary to practice the invention.

Applicant respectfully disagrees with the Examiner's position. First, and contrary to the Examiner's position, applicants note that the breadth of claims 1-6 is relatively narrow, in that they provide only chimeric proteins comprising a DNA methyltransferase

whose DNA-binding activity is attenuated relative to naturally occurring DNA methyltransferase (as opposed to "any DNA methyltransferase ..." as stated by the Examiner) and a DNA binding protein linked thereto that binds to the gene's promoter sequence under conditions permitting the methylation of a methylation site in the promoter sequence of the gene (as opposed any "DNA binding protein ... that binds to a gene's promoter sequence") to permit methylation of a methylation site within the promoter. For the same reasons just recited, the breadth of claims 11-14, 18, 24-26 and 44-46 is also relatively narrow.

Second, applicant maintains that the specification provides adequate guidance for practicing the claimed invention. That is, the experiments in the specification at, *inter alia*, page 44, line 24 to page 47, line 12, and page 52, line 34 to page 54, line 13, showing working examples of the chimeric proteins, combined with a detailed description of methods for designing and selecting of other protein chimera, would enable one to practice the invention as claimed without undue experimentation. Thus, appropriate guidance is provided by the specification.

Third, contrary to the Examiner's position, the ability to isolate proteins or nucleic acids encoding proteins with altered functionality is not highly unpredictable. The Examiner's position appears to be based on his assertion that applicant has not provided a list of specific amino acid modifications and detailed description of the ways the protein structure relates to its function. The Examiner also asserts that it is not routine in the art to screen for modifications having the desired functionality. Applicant submits that contrary to the Examiner's position, applicant has fully described in the specification the requirements for obtaining the chimeric proteins as encompassed by the claims. In addition, applicant's description of the

design, selection and screening of other chimeras is sufficient for the purposes of enablement. The Examiner's assertion that the specification corroborates this alleged unpredictability is incorrect. The statement cited by the Examiner in support of this assertion does not relate to an alleged unpredictability in generating mutants, but relates to using random mutagenesis. Also, applicant's statement in the specification that it may be necessary to perform more that one iteration of the mutagenesis/selection process does not provide corroboration for the alleged unpredictability, but is merely a statement as to the quantity of routine experimentation that may be required. The fact that a larger quantity of experimentation may be required to practice the invention does not mean that it is not enabled, as long as such experimentation is not undue.

Fourth, regarding the Examiner's rejection of claims 44-46, it appears to applicant that the Examiner objects to the intended use of the claimed pharmaceutical composition. The Examiner's belief that such pharmaceutical composition would not be effective in treating a disease has not been adequately supported. That is, the Examiner has not shown evidence that would support a position of lack of enablement for these claims.

Applicant therefore maintains that the rejected claims are enabled.

In view of the above remarks, applicant respectfully requests that the Examiner withdraw the rejection of claims 1-8, 10-15, 18, 24-26 and 42-46 under 35 U.S.C. §112, first paragraph.

Conclusion

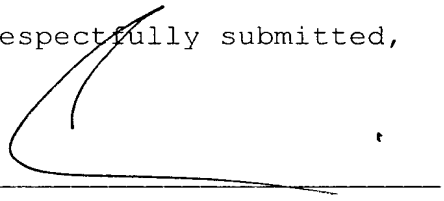
Applicant maintains that the pending claims are in condition for

allowance, and thus, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicant's undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the enclosed $475.00 extension fee, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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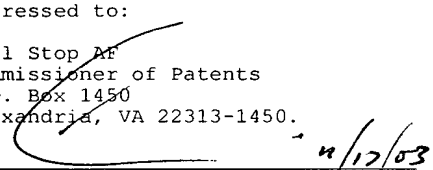

11/17/03
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